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**ISSUE FEE TRANSMITTAL LETTER**

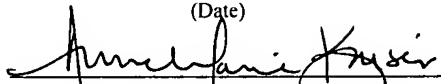
Applicant : Goddard et al.
App. No : 10/063,599
Filed : May 3, 2002
For : SECRETED AND TRANSMEMBRANE
POLYPEPTIDES AND NUCLEIC ACIDS
ENCODING THE SAME
Art Unit : 1647
Class/Sub-Class : 530-387100
Examiner : Sandra L. Wegert

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

October 25, 2006

(Date)


AnneMarie Kaiser, Reg. No. 37,649

MAIL STOP ISSUE FEE

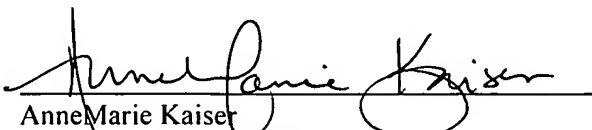
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing is the Issue Fee for the above-identified application:

- (X) Comments on Statement of Reasons for Allowance.
- (X) Form PTOL-85.
- (X) A check in the amount of \$1,730 is enclosed for the following fees:
 - (X) \$1700 Issue Fee
 - (X) \$300 Publication Fee
 - (X) \$30 Advance Order of 10 Copies
- (X) Return prepaid postcard.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 11-1410.


AnneMarie Kaiser
Registration No. 37,649
Attorney of Record
Customer No. 30,313
(619) 235-8550



GNE 230R1C72

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Goddard, et al.
Appl. No. : 10/063,599
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AnneMarie Kaiser, Reg. No. 37,649

COMMENTS ON STATEMENT OF REASONS FOR ALLOWANCE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants received a Notice of Allowability and Examiner's Statement of Reasons for Allowance mailed from the USPTO on September 5, 2006. Applicants submit the following Comments on the Examiner's Statement.

The Examiner's Statement includes the following:

Applicant relies on more than 140 references (see IDS filed 16 June 2006), where expression levels of mRNA, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels.... While the PTO found several references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR, the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels. Applicant asserts that the expression levels of protein correlate to mRNA (cDNA) levels when the cDNA is measured by quantitative PCR (i.e. RT-PCR). Applicant has provided more than 140 references in support of this position. *Notice of Allowability* at 3-4 (citation omitted).

Appl. No. : 10/063,599
Filed : May 3, 2002

Applicants have submitted as exhibits numerous references in support of their assertion that, generally speaking, differential mRNA expression levels (e.g., tumor tissue vs. normal tissue) result in similar differential expression levels of the encoded protein. In addition, Applicants have submitted several Information Disclosure Statements listing numerous additional references, including those submitted as exhibits. Applicants have not represented to the PTO that all of the references submitted to the PTO in an IDS support Applicants' assertions. Applicants have also argued that statements by the authors of Hu *et al.* (J. Proteome Res. 2003; 2(4):405-12) regarding the significance of differential mRNA expression detected by mRNA microarrays are not relevant to the data relied on by Applicants. Applicants' data in Example 18 of the instant application are based on RT-PCR, which is recognized by those of skill in the art as more sensitive and reliable than mRNA microarrays, and therefore the opinions of Hu regarding the significance of differential mRNA data from microarrays is not relevant to the instant application. Applicants' have not argued that microarray data are not reliable, or that all of the supporting references relied on by the Applicants' used quantitative RT-PCR to measure mRNA levels.

Finally, Applicants note for the record that they do not necessarily agree with the PTO's characterization of the references cited in the Examiner's statement of reasons for allowance. Applicants do agree with the PTO's conclusion that "[b]ased on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by RT-PCR would be predictive of an increase in protein expression levels, absent evidence to the contrary."

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Oct. 25, 2006

By: AnneMarie Kaiser

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